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Sulphanilamide in the Treatment of Bovine Mastitis due to Str. agalactiae, with Coincident Observations on the Value of Irrigation with Euflavine in Lactose Solution

By

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The purpose of this report is to give (1) the results of some preliminary experiments made to find out whether sulphanilamide was likely to be of any value in the treatment of the common chronic form of bovine mastitis due to *Str. agalactiae* and (2) the results of a field trial based thereon in which some coincident observations on the value of udder infusion with euflavine in lactose solution were also made. The preliminary experiments were carried out in the Division of Preventive Medicine of the Royal Veterinary College and followed earlier observations on the blood and milk concentrations produced in different animals by various scales of dosage (Stableforth, 1938, 1939; Stableforth and Hignett, 1942). The field trial was a co-operative effort made between 1938 and 1941 by six laboratories in six separate areas of England and Scotland.

The work as a whole was sponsored by the Agricultural Research Council and the field trial by its Mastitis Committee. The general plan for the field trial was laid down beforehand in order to ensure so far as possible uniformity in dosage, methods and criteria of infection and cure. In both the preliminary experiments and in the field trial observations were continued for a period of at least three months after treatment. Bacteriological results are available for all cases. Clinical results are available for only a proportion of the cases because the work was originally planned to assess bacteriological or complete cures and only expanded to include clinical cures when it was realised that a considerable number of cases were cured in the clinical sense although they still remained infected with *Str. agalactiae*.

Reports on the treatment of bovine mastitis by means of sulphanilamide have now been made by a number of workers. Allott (1937) treated three old chronic cases due to haemolytic streptococci with relatively small doses and reported marked clinical improvement. Stevens (1937), quoted by Johnson and Miller (1938), treated three cases due to streptococci with small doses and reported clinical and bacteriological cures in all. Ramsay (1938) treated two acute cases and reported clinical cures in both. Schalm (1938), quoted by Gildow, Fourt and Shaw (1938), treated four cases of streptococcal mastitis and reported improvement but only temporary disappearance of the streptococci. Schlotthauer (1938), also quoted by Gildow, Fourt and Shaw, treated a case of streptococcal mastitis and reported only temporary inhibition of the streptococci. Johnson and Miller (1938) treated ten *Str. agalactiae* cases, six with small and four with moderate doses and reported no useful effect. Gildow, Fourt and Shaw (1938) treated 16 streptococcus cases with approximately 1 gramme per 20 or 10 lb. body weight respectively and reported relief of the clinical symptoms in eight out of nine acute cases and in four old chronic cases but no bacteriological cures. Klein, Kleckner, Scheidy and Craige (1938) treated eight *Str. agalactiae* cases with small doses, sufficient to give only 1 or 2 mg. per cent., and reported cure of one latent case, and relief of clinical symptoms with reduction of cell count and streptococci in the other cases. Bauer and Gunderson (1938) treated eight cases of chronic streptococcus mastitis with various doses and reported only temporary reduction of the streptococci. Miller, Mingle, Murdock and Heishman (1939) treated two streptococcus cases with large doses and reported cure of one. Hoge, Halversen and Cherrington (1939) treated five cases with doses sufficient to give milk concentrations of 5 to 8 mg. per cent., and reported improvement of one acute case, but only temporary effects in the other cases. Miller, Murdock and Heishman (1939) treated three *Str. agalactiae* cases with large doses and reported that the streptococci were not permanently removed. Little (1939) treated five *Str. agalactiae* cases with reduction of symptoms and cell counts but without elimination of the streptococci. Klein, Kleckner and Parry (1939) treated 20 cases of *Str. agalactiae* mastitis and one case of staphylococcus mastitis with moderately large doses, and reported cure of two acute cases and of the staphylococcus case but only temporary reduction of the streptococci in the others. Stevenson 1939) treated ten streptococcus cases with small doses and reported that the streptococci were not eliminated. Bryan and Arnold (1940) treated 16 streptococcus cases presumably *Str. agalactiae*), five with small doses and no useful effects, and eleven with moderate to large doses of which two, acute cases, were cured and the remainder only showed a temporary reduction of the streptococci. Heishman and Miller 1940) have also reported *in vitro* experiments on *Str. agalactiae* which will be referred to later.

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Part I—Preliminary Experiments

In these experiments three scales of dosage were tried successively, *viz.*: (1) three doses of 1 gramme per 5 lb. body weight (360 grains per cwt.) at intervals of 48 hours, (2) an initial dose of 1 gramme per 5 lb. body weight (360 grains per cwt.) followed by maintenance doses of 1 gramme per 10 lb. body weight (180 grains per cwt.) at intervals of 24 hours for six days and (3) an initial dose of 1 gramme per 5 lb. body weight (360 grains per cwt.) followed by maintenance doses of 1 gramme per 30 lb. body weight (60 grains per cwt.) at intervals of eight hours for six days. The sulphanilamide was given in suspension in water by drenching or by stomach tube. The latter method was used in order to ensure accurate dosage. In the result, however, no significant difference could be observed in the concentrations of sulphanilamide reached or in the therapeutic effects. Estimations of the concentrations of sulphanilamide present in the milk were made in all cases. These have already been reported as part of general observations on the concentrations present in the blood and milk of various species (Stableforth, 1939; Stableforth and Hignett, 1942). The more important findings may, however, be recalled :– (1) a dose of 1 gramme per 5 lb. body weight produced a mean milk concentration of $15{\cdot}68 \pm 2{\cdot}84$ mg. per cent. (mgms. per 100 c.c.) at eight hours after dosing, $9{\cdot}16 \pm 3{\cdot}95$ mg. per cent. at 24 hours, and $1{\cdot}77 \pm 1{\cdot}08$ mg. per cent. at 48 hours; repetition at 48 hours produced much the same sequence of concentrations, (2) an initial dose of 1 gramme per 5 lb. body weight followed by 1 gramme per 10 lb. body weight at intervals of 24 hours resulted in the maintenance of a mean milk concentration fluctuating between $13{\cdot}26 \pm 2{\cdot}70$ at eight hours after dosing and $9{\cdot}16 \pm 2{\cdot}44$ at 24 hours after dosing, (3) an initial dose of 1 gramme per 5 lb. body weight followed by maintenance doses of 1 gramme per 30 lb. body weight every eight hours resulted in a fairly level mean concentration of $11{\cdot}01 \pm 5{\cdot}12$ during the period of treatment. All these figures are means and individual cows varied considerably.

Bacteriological Methods and Criteria of Infection before and after Treatment.—Most of the cows used for these experiments were in herds in which regular cultural examinations of milk samples were being made with a view to the control of the disease so that the history of the cow and herd over a considerable period was already known.

Milk samples were plated in crystal-violet aesculin blood agar (Edwards, 1933) centrifuge deposit being used. Cows were chosen which had shown clear evidence of infection in at least two tests, the last within 14 days (usually seven days) before treatment. Post-treatment tests included three tests covering a period of at least three months after treatment was completed. No cow was regarded as cured unless the results of all three of these tests were negative.

The cows treated were representative of all stages of the disease from definite infection without clinical symptoms to old standing cases with marked clotting of the milk or in some cases induration. The average number of infected quarters was about two per cow.

Results

The results of these preliminary experiments are shown in Table I. It will be seen that the proportion of cures rose from 6·4 per cent. for 48-hourly treatment, to 22·2 per cent. for 24-hourly treatment

TABLE I

Preliminary Experiments on Treatment of *Str. agalactiae* Mastitis by means of Sulphanilamide. Bacteriological results

	Treated	Cured	Percentage
48-*hour interval*: 3 doses of 1 gramme per 5 lb. body weight (360 grains per cwt.)	47 cows (in 5 herds)	3 cows	6·4
24-*hour interval*: initial dose 1 gramme per 5 lb. body weight (360 grains per cwt.) Five doses of 1 gramme per 10 lb. body weight (180 grains per cwt.)	36 cows (in 4 herds)	8 „	22·2
*8-*hour interval*: same initial dose; 15 doses of 1 gramme per 30 lb. body weight (60 grains per cwt.)	23 cows (in 2 herds)	11 „	47·8

* Of these 23 cows, 9 had resisted attempts at cure by another method. Excluding these the figures were 14 treated, 8 cured, 57·1 per cent.

and 47·8 per cent. for eight-hourly treatment (or, excluding some animals which had already resisted treatment by other methods, to over 50 per cent.).

It may be remarked here that these scales of dosage were the highest which could be used without causing serious disturbance of health and reduction of milk yield and that even these doses caused marked diarrhoea and/or a definite drop in milk yield in many cows.

The presence of infection in all four quarters, a history of old-standing infection or marked clinical symptoms all appeared to reduce the chances of cure but the numbers are too small for the effects of these characters to be separately assessed. The average type of case treated by the three methods was, however, similar so far as could be ascertained except that it was less severe in one of the herds in which eight-hourly treatment was carried out.

On the basis of these results it was decided to carry out a large-scale field trial adopting the eight-hourly scheme of dosage, treatment being continued for five to seven days. It was also decided to explore the possibility of treating cows for a prolonged period, 15 days.

Part II—The Field Trial

As already stated the field trial included observations on the value of oral treatment with sulphanilamide and udder irrigation with euflavine in lactose solution. For this purpose it was originally intended that in each area and, as far as the number of cows allowed, in each herd there should be an equal number of controls and cows treated by each of the methods, but for various reasons this could not always be done. Sulphanilamide treatment for five to seven days was used on all farms; the test of 15-day sulphanilamide treatment was abandoned early in the trial for reasons which will later be given, whilst euflavine treatment could only be used in a small number of the herds.

The Grouping of the Cows.—In most of the herds regular cultural examinations of milk samples were being carried out with a view to the control of the disease so that the history of the cow was in these cases already known over a considerable period. In other cases the necessary examinations were made before treatment commenced. The cows were then divided into the requisite number of comparable groups to act as controls or be treated by one or other method. In forming these groups attention was paid particularly to the number of quarters infected, the period during which the cows were known to have been infected, the presence or absence of clinical symptoms, and finally, the mastitis history and milk yield. Where this could not be done in individual herds owing to the small number of infected cows, the groups were balanced as far as possible amongst the cows treated by a given laboratory.

Bacteriological Methods and Criteria of Infection before and after Treatment.—In all cases milk samples were plated in crystal-violet aesculin blood agar (Edwards, 1933). In some cases centrifuge deposit was used, in some cases whole milk, in others gravity cream. The same method was, however, used by each laboratory for its own treated or control cows. Pre-treatment tests included at least two strongly positive results (100 or more typical colonies of *Str. agalactiae* from 0·5 c.c. of whole milk or its equivalent), the last positive result being obtained within 14 days before treatment.

Post-treatment tests included at least three tests covering a period of three months after treatment was completed, one of which was carried out in a liquid enrichment medium. Post-treatment tests were in this respect more severe than pre-treatment tests. In many cases they also covered a period considerably longer than three months. No cow was regarded as bacteriologically cured unless negative results were obtained to all three tests.

Records were kept of clinical symptoms during the three months after treatment and also in many cases of milk yields.

Dosage of Sulphanilamide.—Sulphanilamide was given in suspension in water by drenching. The initial dose* was 1 gramme per 5 lb. body weight, the maintenance doses 1 gramme per 30 lb. body weight every eight hours. In the main group of treated cows this rate of dosage was continued for five to seven days. In a small number of cows the treatment was continued for periods up to 15 days.

Euflavine by Udder Infusion.—Euflavine was used at a concentration of 1 : 10,000 made up in 4 per cent. lactose solution. The method of irrigation was similar to that used by Stableforth and Scorgie (1938), *i.e.*, the quarter was milked thoroughly, washed out quickly by injecting a small volume of the solution and stripping immediately and filled at once to a tension† similar to that present at milking time. The solution was left in overnight in dry cows. In lactating cows it was stripped out as thoroughly as possible at once and several times in the succeeding 24 hours. One infusion only was given except at Compton where two were given with an interval of eight days.

Results

Detailed records of each cow were kept at the various centres but considerations of space prevent full reproduction here. The results of the trial as a whole are summarised in Table II. The small number of cows treated with sulphanilamide for 15 days as already stated is due to the fact that this method was abandoned early in the trial because many cows developed serious toxic symptoms after eight or more days of treatment. More detailed results for the five to seven days sulphanilamide treatment are given in Table III on account of the relatively large number of cows treated by this method and to show the diversity in the results obtained at the several centres and the bearing of the presence or absence of clinical symptoms on the results. The results in Tables II and III include the 23 cows treated by the same method in the preliminary experiments reported in the earlier part of this paper.

Table II

Field Trial (Summary of Results). Various Methods

	Bacteriological Results		Clinical Results	
	Treated	Cured	Treated	Cured
Controls	175	10 (5·7 per cent.)	31	3 (9·7 per cent.)
Sulphanilamide 5-7 days *per os*	299	104 (34·8 per cent.)	134	74 (55·2 per cent.)
Sulphanilamide 15 days *per os*	29	6 (20·7 per cent.)	7	4
Euflavine in lactose (1 infusion)	72	30 (41·7 per cent.)	No data	

Cure in the case of controls means recovered spontaneously.

Cure in the case of bacteriological results means the animal became negative and remained negative for at least three tests over at least three months.

Cure in the case of clinical results means that the milk of one or more quarters which was unusable before—clotted or pus-like—became normal and remained so for at least three months. Marked improvement, *i.e.*, clinical cure of one or more quarters of an animal affected in several quarters, or cure of all abnormal quarters for a shorter period than three months was reported in an additional 27·9 per cent. of 61 cases (data not given for other cases).

Bacteriological Results.—It will be seen from Table II that 5·7 per cent. of the 175 controls recovered without treatment, whilst the number which became negative after treatment was 34·8 per cent. for the 299 cows which were given sulphanilamide for five to seven days, 20·7 per cent. for the 29 cows which were given sulphanilamide

* At the Hannah centre the initial dose was 1 gramme per 10 lb. body weight.

† Further experience has shown that this tension is too great and that the clinical reaction to udder irrigation is reduced by injecting a smaller volume.

Table III

Sulphanilamide 5 to 7 days

Centre	Number of Herds	Number Treated	Average Quarters Infected	Bacteriological Results						Clinical Results	
				Latent Cases		Clinical Cases		Total Cases			
				Treated	Cured	Treated	Cured	Treated	Cured	Treated	Clinically Cured
London	7	64*	1·8	36	19 (52·5)	10	4	64	30 (46·8)	10	4
Hannah	28	132	2·2	68	33 (48·5)	64	18 (28·1)	132	51 (38·6)	64	44 (68·7)
East of Scotland College	6	15	..	7	1	8	1	15	2	8	4
Compton	1	9	2·3	6	1	3	1	9	2	3	1
West of Scotland College	1	9	..	..	..	..	..	9	2	..	..
Leeds	13	46	2·1	38	4	38	7 (18·4)	46	11 (23·9)	38	20 (52·6)
Wye	5	24	2·5	13	4	11	2	24	6	11	1
	61	299		138	62 (44·9)	134	33 (24·6)	299	104 (34·8)	134	74 (55·2)

For explanation see legend to Table II, "Latent case" means that the milk showed no clots or other obvious abnormality; it may have shown an abnormal deposit after centrifuging.

Figures in brackets are percentages.

* The data showing whether eighteen of these cases were latent or clinical are unfortunately not available.

for 15 days and 41·7 per cent. for the 72 cows treated by udder infusion with euflavine in lactose solution.

The further details given for five- to seven-day sulphanilamide treatment in Table III show that the proportion of latent cases in which a bacteriological cure was obtained was 44·9 per cent. as compared with 24·6 per cent. of clinical cases.

Clinical Results.—The figures in Table II show that whereas clinical symptoms disappeared spontaneously in 9·7 per cent. of the clinical cases left as controls, treatment with sulphanilamide for five to seven days was followed by the disappearance of clinical symptoms in 55·2 per cent. of cases. Comparison of this figure with that for bacteriological cures in clinical cases (Table III) shows that in many cases the clinical manifestation disappeared although infection remained. Disappearance of clinical symptoms was often dramatic and occurred within a day or two ; in other cases return to normality was more gradual. Cows are only included in the tables as clinically cured if recovery was complete and lasted for the period of three months laid down. In an additional 27·9 per cent. of 61 cases for which the requisite data are available partial recovery occurred, *i.e.*, the symptoms disappeared from one or more quarters of a cow affected in several quarters, or were absent for a period of less than three months.

Toxic Symptoms and Milk Yield.—A detailed description of the symptoms produced in the cows concerned in Part I of this paper formed part of the previous report dealing in general with the use of sulphanilamide in animals (Stableforth and Hignett, 1942). The symptoms seen in the remaining cows were in essential respects similar to those already reported. It will therefore suffice to recall the outstanding observations. The most common symptoms were some sleepiness and inco-ordination of movement, closely associated with high blood concentrations of sulphanilamide, some anorexia, diarrhoea, often marked and a drop in milk yield. Effects varied widely, however, a large proportion of cows showing no ill effects whatever or only mild effects of no practical importance. Others, however, showed pronounced symptoms including severe diarrhoea at some time during the period of dosing or throughout, and a serious drop in milk yield. Comparison of the recorded milk yields of treated and untreated cows showed that, whilst the yield in certain cases dropped 40 per cent. during the week of dosing and was still 20 per cent. below normal the following week, other cows showed no drop whatever. The average loss of milk attributable to sulphanilamide worked out at 18 per cent. for the week of treatment and 9 per cent. for the following week, yields thereafter being normal.

Prolongation of treatment produced no ill effects in many cows but in others was followed by marked toxic effects which usually developed rather suddenly and included marked or complete anorexia, a general tucked-up appearance, haggard eye, cold extremities, a dry scaly nose, some degree of jaundice, a weak pulse and a further drop in milk yield. Dosing was in such cases stopped at once and recovery was rapid though milk yields never returned to normal.

Discussion

At the time the trial was arranged it was already known that *Str. agalactiae* could be eliminated from the bovine udder in a high percentage of cases by irrigation with one or other of the acridine dyes. It had also been found that these methods have several disadvantages in common, the chief of which are that they are time consuming, and therefore relatively costly, and are also accompanied by the loss of the whole of several days' milk even when carefully carried out, and by more serious effects if due care is not used and even apparently in some cases where all care is used. It had been shown on the other hand that sulphanilamide could be administered for five to seven days at a dosage rate sufficient to give a milk concentration of about 10 mg. c.p., with safety and with an average loss of milk amounting to 18 per cent. during the week of treatment, 9 per cent. the following week and none thereafter or a total of about one-quarter of a week's yield ; whilst preliminary experiments on a limited number of cows had suggested that by such treatment the streptococci could be eliminated in a considerable proportion of cases. The field trial was so arranged therefore as to give first place to an assessment of the value of this method on a large number of cows in various herds and in several areas. The number of cows thus treated was 299, and 175 comparable animals were kept as controls.

It will have been observed that the results varied considerably from centre to centre. At each of the larger centres there was a significant advantage (more than twice the standard error) in favour of the treated animals, whilst the totals show that 34·8 per cent. of the treated animals were bacteriologically negative as compared with 5·7 per cent. of the controls, a difference in favour of the treated animals which is nine times its standard error. It may be concluded therefore that the difference was not due to chance. One reason for the variation noted at the several centres would appear to be the proportion of clinical cases amongst the animals treated. Thus, for the three larger centres, London, Hannah and Leeds, the percentages of bacteriological cures were 46·8, 38·6 and 23·9 and these were associated with about 30, 50 and 80 per cent. of clinical cases respectively, whilst the total percentages of cures in clinical and latent cases were significantly different, *viz.*, 24·6 and 44·9 per cent. respectively, with a difference 3·6 times its standard error. Notwithstanding this general finding the percentage of cures did not in all cases follow the proportion of clinical cases, *e.g.*, in one herd a high percentage of clinical cases was associated with cure of most.

Another factor which may also have been in operation is a variation in the susceptibility of the streptococci concerned to sulphanilamide. Support is given to this suggestion by the very marked differences obtained when treating apparently similar groups of cases in different herds. In some herds few or no animals were cured, whereas in others nearly all responded. It is now known that resistant strains exist amongst strains of *Str. pyogenes* (Lancefield group A) and in other species, whilst Long and Bliss (1939) and Heishman and Miller (1940) have reported variations amongst strains of *Str. agalactiae* (Lancefield group B). Hignett and Hughes, D. L. (private communications) have also found resistant strains in this country and Hignett has found some evidence of correlation with the results of treatment.

The proportion of bacteriological cures obtained by the various American workers listed earlier is considerably lower than those reported here. This may have in some cases been due to less adequate dosage, but in others, *e.g.*, Gildow, *et al.* (1938), Miller *et al.* (1939) (1) and (2)), Klein *et al.* (1939), Little (1939) and Bryan and Arnold (1940), the dosage was large and continued for periods as long as or longer than were used here. In no case, however, were really large groups of animals treated and chance or the sulphanilamide susceptibility of the strains concerned may have played a part. Differences in the severity of the method of examination after treatment might also have played some part but there seems no reason for attributing the divergence of results to this factor.

The percentage of cures obtained would seem to be near the maximum to be expected from sulphanilamide treatment in any large group of herds because even if a greater percentage of cures could be obtained by a higher dose rate, such treatment would be precluded by the clinical disturbance and loss of milk which would be a result in many herds. The percentage of cures in the small group to which sulphanilamide was administered for more than seven days does not, moreover, suggest that prolonged treatment would be likely to give better results. The percentage of cures obtained in the group given prolonged treatment in this trial was actually lower, though not to a significant degree.

It seems likely on the other hand, all facts considered, that similar results would have been obtained by reduction of the initial dose to 1 gramme per 10 lb. body weight with the consequent small saving in cost and less disturbance to the cow. This was in fact done at the Hannah centre, where the results were a little above the average and as high as would be expected in view of the proportion of clinical cases treated. It seems also probable that dosing at intervals of twelve hours would have been followed by similar results and even possible that daily dosing would not have affected the results seriously. It is true that the results obtained by daily treatment in the preliminary work were not as good as those obtained by eight-hourly dosing in the preliminary work and in the field trial. The reason for this would not, however, appear to be at all certainly connected with the interval between doses and the sulphanilamide concentrations, since the difference in the percentage of cures was only just significant (it was just twice its standard error) and as shown earlier (Stableforth and Hignett (1942), Figs. 3a and 3b) the milk concentrations during daily dosing were as high as during dosing at intervals of eight hours and did not show a much greater fluctuation.

The bacteriological results obtained with sulphanilamide compare unfavourably with those which have been obtained by udder irrigation with the acridine dyes and also with the results obtained with the more recently introduced drugs, gramicidin and novoxil* with both of which the udder disturbance is also much less than with the acridine dyes. It seems therefore that treatment with sulphanilamide by the oral route cannot be recommended as a routine measure for the elimination of *Str. agalactiae* from the bovine udder.

On the other hand the finding that in over half of the clinical cases treated the symptoms disappeared and remained absent for at least three months, as compared with spontaneous disappearance without treatment in under 10 per cent. of cases (a difference of 6·5 times the standard error), shows that sulphanilamide has a definite place in the treatment of clinical cases. Since, however, it is known that in most of these cases the streptococci still remain, it must be expected that clinical symptoms will eventually recur, at least in many cases; though experience seems to suggest that, once the balance has been

* For further information regarding these drugs see annotation by Edwards, S. J.—this journal and Volume p. 499.

tipped, the animal's own resistance is often such that clinical symptoms may be suppressed for a considerable time and there is some evidence to suggest that an animal which is still infected shortly after treatment may after some weeks or months itself get rid of the streptococci. Further information on this point would be of interest, but could only be obtained by regular bacteriological examination of a large number of treated and untreated cows over a long period.

It was originally intended that the cases treated should be in every respect a representative cross-section of *Str. agalactiae*-infected cows. The high proportion of clinical cases, particularly at certain centres, suggests, however, that the cases treated were on the whole of more than average severity. One reason for this is probably the fact that in the process of ensuring that animals were firmly infected before inclusion in the trial there was inevitably some selection of the more severe cases.

The results obtained by the irrigation method used here (1 : 10,000 euflavine in lactose) do not suggest that this method is worth pursuing, because the recovery of the injected solution was not better than is the case with watery solutions nor was the udder disturbance less, whilst the 41·7 per cent. of cures is considerably lower than has generally been obtained by other irrigation methods.

Summary

Observations are reported on 658 cows infected with *Str. agalactiae* of which 411 were treated by the oral administration of sulphanilamide, 72 were treated by udder irrigation with euflavine in lactose solution and 175 were held as controls. The cows were in 61 herds situated in six areas of England or Scotland and were firmly infected before treatment began. In reporting the results the terms "bacteriologically cured" and "clinically cured" are used. The former implies that a minimum of three samples were examined after treatment, that they covered a period of at least the three months period laid down and that *Str. agalactiae* was not recovered. The latter term implies that the milk was abnormal before treatment in one or more quarters and that after treatment it became normal and remained so for at least three months.

Sulphanilamide

Of 47 cows given three doses of 1 gramme per 5 lb. body weight (360 grains per cwt.) at intervals of 48 hours, 6·4 per cent. were bacteriologically cured.

Of 36 cows given an initial dose of 1 gramme per 5 lb. body weight (360 grains per cwt.) followed by five further doses of 1 gramme per 10 lb. (180 grains per cwt.) at intervals of 24 hours, 22·2 per cent. were bacteriologically cured.

In clinical cases in the above two groups clinical cure or marked improvement usually followed.

Of 299 cows given an initial dose of 1 gramme per 5 lb. body weight (360 grains per cwt.)—or in 132 cases half this initial dose—followed by further doses of 1 gramme per 30 lb. (60 grains per cwt.) at intervals of eight hours for five to seven days, 34·8 per cent. were bacteriologically cured; 44·9 per cent. of the latent cases and 24·6 per cent. of the clinical cases. Of the clinical cases 55·2 per cent. were clinically cured, whilst definite improvement occurred in a further 27·9 per cent. of cases.

Of 29 cows dosed at the same rate as the last group but in which dosing was continued for up to 15 days, 20·7 per cent. were bacteriologically cured. This prolonged treatment was not pursued owing to the serious toxic effects in some cows.

Irrigation

Of 72 cows treated by udder irrigation with 1 : 10,000 euflavine in 4 per cent. lactose solution, 41·7 per cent. were bacteriologically cured. The udder reaction was not less than has been reported for various acridine dyes in aqueous solution and the percentage of cures was lower.

Controls

Of 175 cows held as controls under the same condition as the above treated cows, 5·7 per cent. became bacteriologically negative. Of 31 clinical cases for which the data are available, 9·7 per cent. became normal.

Attention is drawn to the marked divergence in the results obtained in different herds and the fact that this did not always follow the proportion of clinical cases.

It is concluded that oral treatment with sulphanilamide cannot be recommended as a routine method for the elimination of *Str. agalactiae* from the bovine mammary gland, but that it has a definite place in the treatment of the associated clinical symptoms, and that for this purpose an initial dose of 1 gramme per 10 lb. body weight (180 grains per cwt.) followed by half this dose at intervals of about 12 hours for a few days provides a suitable scheme of dosage.

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MINISTER ON MILK AND OTHER MATTERS

Addressing an audience of farmers and other land workers at Carlisle on December 14th, Mr. R. S. Hudson, Minister of Agriculture, said that milk, particularly winter milk, was a first priority. He congratulated Cumberland on appearing at the head of the Northern League in the Victory Churn Contest, and said that the increase in the dairy herd and particularly autumn calvers was very encouraging, but the main test would come in December. For every gallon of milk sold in January this year Cumberland had sold two in June. That had to be altered in war-time. Winter milk was the essential. Something like half our total milk supply in mid-winter was required to meet the needs of the priority classes of consumers, and the demands of those consumers would be higher this winter than last.

Turning to the important subject of milk recording, Mr. Hudson informed the meeting that a survey of dairy farms in a number of counties had shown that many herds were poorly managed. Inefficiency often occurred because farmers did not know the yield of individual cows, and unless they knew that there was no basis for efficient feeding. The Minister said that although he had been pressed to introduce a national system of compulsory recording he had decided that better results were likely from the voluntary principle. The Milk Marketing Board, in agreement with the Ministry, were launching a simple system of milk recording and he hoped that thousands of dairy farmers would join in. He had no sympathy with a farmer who did not know the output of his cows. "It must be like driving a car without a petrol gauge and without a speedometer."

In the course of his speech Mr. Hudson stressed the advantages of polled cattle: there was a very marked difference in the prices for polled and horned bullocks. Polled cattle could be kept thicker in the yards, required less trough room and made better use of food consumed. The time had come to consider the advisability of dehorning all non-pedigree male calves except those being reared for service. De-horning must be done before a calf was a fortnight old, and under modern methods was painless.

In a reference to one of the most pressing agricultural problems of the day, the Minister asserted that the Government recognised that hill sheep farming was an important item in large parts of Northern England, and that conditions during the last two seasons had adversely affected hill sheep farmers. For these reasons the Government had given a subsidy for ewes of hill breeds kept according to recognised practices, with the object of helping farmers to maintain foundation stocks. A subsidy would be paid for a third year and details would be announced in a few days. Assistance would also be given to farmers who kept hardy cattle on hills for a minimum period of six months, on somewhat similar lines to the scheme already operating in Scotland. There would be a flat rate of £3 a head. All this was complementary to the hill sheep subsidy and part of the Government's plan for dealing with marginal land and farms.

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The Germans have ascertained, by measurement, that the food utilisation, working capacity, endurance and respiration during long periods of work are greatest in horses whose chest girth (measured round the thorax and over the highest point of the withers) considerably exceeds height at withers. They state that horses with a difference of less than 20 cm. (about 8 in.) in the two measurements are unsuitable for hard work.—*N.H.A. News Sheet.*

CLINICAL COMMUNICATION

Cramp in the Greyhound

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The article by Mr. Male on the above subject is of great interest to all whose work brings them into contact with the greyhound, and the author is to be congratulated on his valuable contribution. He has endeavoured to sift the relevant from the irrelevant material, but, in my opinion, has discarded some that ought to have been retained, and over-emphasised strychnine as a real cause of cramp.

Cramp in the greyhound is that rigid contraction of groups of muscles—generally in the thighs or shoulders, but also very occasionally in the loins—which occurs when the animal is at full gallop. The affected limb becomes rigid, ceases to be capable of forward movement, and drags behind. The animal endeavours to continue his gallop, but becomes increasingly affected, more distressed, and falls over. Though I recognise cramp as arising from four distinct causes, *viz.* unfitness, weather, fretting (temperament) and drugs, it would seem to be more suitable to consider the condition under two main groups—(I) Physiological Cramp, *i.e.*, cramp which arises from unfitness, weather or fretting, and (II) Cramp due to Drug administration.

Group (I).—Physiological Cramp.—In group (I) are the types which really concern us as a veterinary or medical condition of great interest, and it is important that the difference in the two groups should be clearly recognised, so as to avoid all doubt regarding onset of symptoms and treatment applied. Mr. Male has already unfortunately misinterpreted the bromide treatment and the type of case in which it has been applied successfully. In all cases of group (I) cramp the attack may last from five to ten minutes, sometimes less, but never longer. It does not recur when the animal is at rest, and can only be reproduced following a sequence of events similar to that which preceded the original attack.

(*a*) *Cramp due to unfitness* is common, and has been described by Sams and Mrs. Evans. It occurs when the dog is galloped in the early stages of illness. It is seen after a close season when dogs have been denied their usual weekly or bi-weekly gallops for periods varying from a month upwards. The feasible explanation would seem to be that waste products have collected in the muscle tissue, once highly developed (that is important) and now in a state of partial disuse. The animal is released after an artificial lure and enticed to travel for a distance which his musculature is not in a fit state to undertake. The dog travels as far as he can in a normal manner, but the unfit state of his muscles determines the length of his gallop. Beyond that distance he is attacked by cramp and collapses. The cause is physiological and due to normal metabolic changes. It occurs in the absence of all drugs. Treatment is simple and preventive. It consists of a course of gallops over increasing distances until the muscles regain their tone and their original state of development.

(*b*) *Cramp due to weather conditions* is more rare, and probably confined to atmospheric temperature. Heat does not appear to be a cause of cramp in the greyhound, and it seems possible that cramp due to cold atmospheric conditions only occurs in the presence of a low degree of unfitness, which in itself would not have caused cramp over normal distances. Nevertheless, since cold is the factor which decides the issue, it is worthy of note, but it should be stated that it is unlikely to cause cramp in a normal, thoroughly fit dog.

(*c*) *Cramp due to Fretting—Temperamental Cramp*—is the true cramp of the greyhound, and the type which is of the greatest interest. It seems likely that the whole routine of kennel life, including diet, has to be explained before we can really appreciate why the animal takes cramp at the gallop. On an average, not more than one in five hundred dogs is likely to be affected and only dogs of a certain temperament are subject. He is invariably a highly strung, "shivery" individual, and not prone to incessant barking. As speedy as his fellows, he would live under natural conditions. With others of the canine species he would rest, move about, and excrete at will, and be able to travel at full speed over varying distances without taking cramp. Having been put in a training kennel, he gets the usual sloppy food and is frequently exercised each day. On any day he may be transported twenty miles and released after an artificial hare, and he performs creditably. On a racing day, however the routine alters. He is taken his twenty miles, but he is kennelled in a small-sized compartment with a comfortable bed. He hears other dogs going out and awaits his turn apprehensively. He may move very little, apart from his nervous shaking, and he barks, as a rule, considerably less than his fellows in neighbouring kennels. It is certain that he has excreted no urine whilst shut up. After two or more hours of suppressed excitement his turn comes for a race, and he appears to be normal. He excretes some urine and walks for about ten minutes, but when he joins in the race he is invariably attacked by cramp before he has completed the course. The sequence of events can be repeated without variation each week. The dog will always run a trial gallop in the absence of being kennelled up, and always go well. Even if kennelled for an hour, he will still go well, but he is often a dog of too much pace to allow him to run in the lower grade first races, and he has to run later in the programme. Each time he will collapse. It is my view that the nervous tension, coupled with inability to excrete, are the sole causes of the complaint. After all, he drinks some six pints of fluid every day, so that he has much urine to excrete. Dogs kennelled in neighbouring kennels receive the same racing treatment, but behave differently. Some dogs bark and jump up for the whole of the period, but are little the worse. Others again salivate profusely at the door of their kennels, and it may surprise many to know that there are times when one can see a stream of ten or twelve feet of saliva running from a door. The dog doing that is not usually subject to cramp. He may look tired, but runs creditably and completes the course. The cramp dog, however, looks quite well, but runs badly. There is no question whatever of drugs in such cases, and in my opinion the condition bears a close resemblance to "Non-sweating Disease of Horses" in India, as described by Dr. Edwards. Both conditions appear to be due to failure or inability to excrete waste products from the system of the affected animal. The difference lies in the fact that local conditions decree that the horse never gets a start to gallop, whereas the dog starts but cannot continue. Treatment has been disappointing until recently. The condition can be ameliorated, and in some cases actually prevented, by giving a good gallop earlier in the day of racing, and allowing ample time for excretion. It can be prevented by cutting down the time of pre-racing kennelling, which is the most unnatural procedure of all for a dog about to be released for a fast gallop. It has been prevented in recent cases in my hands by the administration of pot. bromide daily (7½ grains) over a period of two months. Such treatment does not affect the pace of the animal, but indications are that it is sufficient to lessen the animal's nervous tension whilst awaiting his turn to race. This lessening process allows the dog to rest normally, and it would appear that, because of this lack of nervous stimulation, his muscles do not collect a surfeit of waste products, whose presence are indicated when the dog is attacked by cramp at the gallop.

Group (II).—Cramp due to Drug Administration is certainly known to appear, and Mr. Male rightly stresses circumstances which are always highly suspicious. I am indebted to him for his description of cases due to a mixture of strychnine, cocaine and heroin. It will be obvious, from what I have said above, that any drug which increases the excitement of the dog is liable to set up cramp, but *in the absence of exercise and excretion only*. In such cases, it is the result of a physiological action. When the "cramp" appears, however, as the result of a drug stimulating the motor nervous system, we encounter a different action, for here the spasm occurs, not as a result of normal waste products accumulating in the musculature, but as the result of the introduction of a definite nerve stimulant into the system. In such cases, according to dosage and absorption, the clonic effect on the muscles may be seen when the animal is at rest and not necessarily when it is caused to gallop. It would appear to be a misnomer to call such cases "cramp."

There is ample evidence to suggest that chloretone is a drug commonly used by the unscrupulous to cause loss of speed and cramp in the greyhound. It seems likely that the cramp symptoms are secondary. The primary intention is to dull the senses of the dog and cause confusion in its mind. The dullness of the senses may inhibit excretion of waste products for some hours, with resultant effect on the muscular system at the gallop. Not all chloretone cases take cramp.

I have no experience of dogs galloping under the effect of morphia, but see no reason to disbelieve the possibility of cramp developing at the gallop if there has been much previous inhibition from any cause whatever.

True cramp in the greyhound has in my definition nothing whatever to do with drugs as a primary cause. The condition arises as the result of definite metabolic changes in the musculature. Stimulant drugs such as strychnine do not cause true cramp, but set up clonic spasms of groups of muscles. Increased excitement will not *per se* cause cramp if free excretion is allowed. Inhibitory and hypnotic drugs are more likely to be a cause of cramp in a dog

(*Concluded at foot of col.* 1, *page* 544)

ABSTRACT

[**GRASS SICKNESS IN HORSES.** A review of the present knowledge of the disease, with particular reference to the nature of the causal agent. Greig, J. Russell. (1942.) *Trans. Highland and Agric. Soc. Scotland.* **54**. 1-27.]

This review consists mainly of an account of the vast amount of work carried out at the Animal Diseases Research Institute, under the direction of Dr. Russell Greig, in an attempt to elucidate the cause of grass sickness. If the aetiology of this condition is still not known it is not for lack of patience or skill on the part of the research team and of the practitioners who have co-operated with them and without whose help little could have been accomplished.

Part I.—Historical and General

The disease was first described as a clinical entity in May, 1911, at a military training camp near Barry and it is unlikely that it existed to any considerable extent prior to this time. Between 1911 and 1920 the disease extended inland and spread northwards, but contiguous areas were not always affected in chronological sequence. Numerous cases have been recorded during recent years in parts of Scotland which were previously relatively free from the disease. Several hundred cases have been recorded in various parts of England but the epizoötic form of the disease is largely confined to the mainland of Scotland and to that area of England lying to the north of a line drawn from Morecambe Bay to Flamborough Head. The striking spread westwards of the disease in Scotland suggested that an infective agent carried by a living vector might be responsible: the causal agent did not seem to be windborne since the prevailing winds in the main area concerned are from the west. Birds were excluded as possible vectors because of the close regional distribution of the disease and the fact that broad rivers such as the Tay appeared to act as barriers to its extension.

The horse appears to be the only susceptible species and susceptibility seems to be equal in all breeds, although some practitioners consider the Shetland pony to possess some degree of immunity. The disease does not occur in suckling foals and is rare in animals under one year but it has been recorded in animals from one year to over 20 years. Among 6,617 insured horses the incidence was highest in animals between three and six years old (5·32 per cent.), the peak being at four years (7·29 per cent.). At other ages the incidence was about 2 per cent. Both sexes appear to be equally susceptible.

The disease is seen mainly in animals at pasture, being rare in stabled animals, even in those fed grass cut from affected pastures. The condition is thus rare in large cities situated within epizoötic areas. Most cases develop when the animals have been grazing the affected pastures for at least a fortnight, although animals have become affected after as short a period of grazing as three days. Cases often occur within a few days of the animals being moved to fresh pastures.

Since horses in the affected areas are usually turned out to grass early in May one would expect the incidence of the disease to rise during the latter part of this month, but in fact the majority of cases of grass sickness occur in June and the incidence falls to a low level by the autumn. During winter and early spring there are a few cases among colts at pasture, sometimes even when there are hard frosts or the ground is covered with snow. During June the disease is usually acute or peracute whereas as the season advances it tends to become more chronic.

No definite correlation with climatic conditions has been traced although some practitioners believe such a correlation to exist and consider that fine, warm, dry weather tends to cause an increased incidence.

Grass sickness occurs at all elevations from sea level to 1,200 feet, under very varied conditions of pasturage, and is seen as commonly on north and east as on south and west exposures. Cases are met with under all conditions of manurial management, including paddocks where no manure is known ever to have been applied. A suggestion that the occurrence of the disease is related to the stage of vegetation in the pasture has not been proven.

The disease was reported in Orkney in 1938, this being the first record of its occurrence on any of the islands. In 1941 it was reported from Northern Ireland.

Farms previously free from the disease may have several cases during one season and then remain free for some time. The distribution of affected farms within a grass sickness area is highly erratic and there is no apparent direct or indirect correlation between one outbreak and another. There is, however, little doubt that there is some fundamental law, as yet undetermined, which governs the case occurrence.

During the summer months the disease often assumes an epizoötic form with an incidence of 2 to 4 per cent. Although only occasional cases are encountered during the winter two or more may occur on one farm at the same time. In 1936 the disease was especially severe and it is estimated that 1,200 to 1,500 horses in Scotland were affected.

Part II.—Clinical and Pathological Features

Symptoms

1. Acute type of disease.

The early symptoms are often indefinite. There is sluggishness and slight abdominal pain, and swallowing is often carried out imperfectly or at least with difficulty. The animal may at first drink normally and then in a few moments it may make retching movements and forcibly eject water from the mouth and nostrils. Food is masticated slowly and attempts to swallow lead to choking and forcible regurgitation of the ingesta. These symptoms appear to be due to oesophageal spasm. The animal soon shows apathy and dejection and even somnolence, from which it can be roused by a sharp word, only to relapse again. The pulse is usually rapid (60 to 80) and soft, and there is sometimes a rise of temperature of about 2 degrees. No faeces are passed. Fine muscular tremors appear over the shoulders and flanks and there is periodic patchy sweating, especially under the tail. The volume of urine passed is almost always considerably reduced and during the whole course of the illness the animal may micturate only once—during the prodromal phase. The bladder is usually found empty at autopsy. Respiration is usually normal in rate but may be laboured: there is sometimes a soft snoring sound. The appetite ceases, there is continuous mental depression which increases in severity and sour-smelling ingesta are regurgitated, sometimes with actual vomiting. Saliva drools from the lips when the mouth is opened but there appears to be no actual excessive secretion. In peracute cases the symptoms may last from twelve hours to three days and they are accompanied by marked distress which seems to be due to acute gastric distension.

2. Subacute and chronic types.

The prodromal symptoms are similar to those of the acute type but much less intense—loss of appetite, sluggish bowel movements, difficult swallowing. The conjunctiva may be icteroid. The animal often stands huddled up in a corner with the hind quarters leaning against the fence. There is seldom any desire to drink. The abdomen becomes progressively contracted, giving the "greyhound" appearance. Subacute cases may continue for one to four weeks, whereas chronic cases may extend for several months and are occasionally followed by apparent recovery. Complete recovery is very rare and animals which appear in good health after a long period of convalescence quickly relapse when put to work.

During recent years the clinical picture of the acute type of the disease appears to have changed, sweating and muscular tremors being now less common than formerly. Recovery from acute attacks seems in recent years to have become more common.

Autopsy Findings

In the acute type there is acute distension of the stomach with fluid, an excess of fluid in the small intestine and acute impaction of the large colon with hard, dry material. No lesion of any organ is constantly found. In less acute and chronic cases the stomach and intestine may be normal. The spleen is usually somewhat enlarged but the pulp is firm. A catarrhal pharyngitis has occasionally been noted.

Extensive investigations over a period of years have failed to reveal any histological changes which are of constant occurrence.

A great deal of biochemical work has been carried out during the past twelve years, especially on the blood, in normal horses and in animals with the various types of grass sickness. In the acute and peracute types the blood picture is suggestive of anhydraemia: studies of the physical characters of the blood confirm this finding. Apart from this the blood picture of affected horses shows no abnormality.

Part III.—Aetiology

General Considerations

There is much to suggest that the causal agent is an infective one but there is also considerable evidence against this view and in support of the hypothesis that the disease is due to a non-viable cause. Thus all attempts to transmit the disease to healthy animals have failed and there is no evidence of direct or indirect contagion under natural conditions. At the same time, two or more cases often appear on the same farm or on neighbouring farms at one time.

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than are stimulants. Above all, we must not confuse strychnine poisoning and its clonic spasms with a single attack of muscular contraction in a muscle or group of muscles in a healthy animal body. Further, we must bear in mind that the almost complete absence of sweat glands has much to do with the appearance of true cramp in the racing greyhound.

Furthermore, the incidence of the disease is highest in animals three to six years old, whilst suckling foals appear to be immune: if an extraneous non-viable toxic substance were responsible one would expect equal susceptibility at all ages. There is a marked age susceptibility in many infective diseases, especially those due to filterable viruses. In the author's opinion the balance of evidence seems to suggest a living infective agent which may, however, be incapable of remaining viable for long periods outside the body of the host. Some insular areas of Scotland have remained free from the disease and here there has been very little importation of horses although there is much human traffic between the islands and the mainland.

The island of Orkney was free from the disease until 1938 when three cases on two farms occurred, followed by three further cases in each of the two succeeding years. All nine cases occurred on farms situated immediately on the coast, although widely separated. In 1940 there were four more cases: these were on inland farms but two of the latter were immediately adjacent to farms on which previous cases occurred.

Horses occasionally recover from grass sickness and such animals have in some cases again developed the disease during the subsequent grazing season. Thus any immunity conferred by one attack can be of only short duration. This is not necessarily incompatible with the view that an infective agent is responsible. Thus, in the case of equine encephalomyelitis, horses which have recovered from one attack may again be affected during a succeeding year.

Possible Aetiological Agents

1. *Plant Poisoning.*—That the disease is due to poisonous plants or to a fungus parasitic on plants was one of the first possibilities which was investigated. Feeding experiments and very extensive botanical surveys have been carried out and these have given no evidence that the pastures of farms where cases of grass sickness occur contain any plant recognised as being even slightly toxic. None of the grasses on such pastures was found to be parasitised by ergot and various moulds which were found at the base of the herbage were fed to horses with negative results. There is thus no evidence that grass disease is caused by poisonous plants or by fungi associated with the herbage.

2. *Deficiency Disease.*—It will be remembered that horses are usually affected with the disease when they have been through the hardest part of the year, doing hard work and fed a diet of oats and hay. The disease does not occur, however, in animals stabled for long periods and other animals may develop the disease only after long periods of grazing. The vitamin A content of the livers of horses dying of acute grass sickness did not differ significantly from that of normal horses. The short course of the acute form of the disease is against the view of a deficiency disease and this hypothesis must be discarded.

3. *Anaphylaxia.*—Most cases of grass sickness develop in animals which have been turned out to grass for at least a fortnight and it has been suggested that during this time the animals may develop a condition of anaphylaxis to some foreign protein. Against this view is the fact that some horses develop grass sickness after being at grass only a few days and that there would in these cases have been insufficient time for the condition of anaphylaxis to develop. Chronic cases also make it difficult to accept this hypothesis of anaphylaxis and there is no suggestion of the nature of the specific protein responsible. Finally, experimental work (unpublished) on anaphylactic shock in the horse has shown a syndrome different from that in acute grass sickness. The balance of evidence is clearly against this hypothesis.

4. *Poisonous Products of Intestinal Origin.*—It has been postulated that the disease might arise from absorption of toxic products elaborated as a result of intestinal stasis. Impaction of the colon appears, however, to be a manifestation of the disease rather than its cause. Again, cases of simple impaction in the horse are common and do not give rise secondarily to grass sickness. Sudden change of diet from oats and hay to succulent pasture has also been suggested as a possible cause but this error of feeding is widespread whereas grass sickness is localised to certain fairly well defined but extending areas. The symptoms of such a change of diet are usually considered to be diarrhoea and a mild attack of colic but they have never been recognised as the precursor of grass sickness. This hypothesis would seem, therefore, to have no basis in either circumstantial or factual evidence.

5. *Toxic Chemical Substances developed in the Pasture.*—Since about 1918, as a result of the use of improved seed mixtures containing wild white clover and because of the increasing use of nitrogenous fertilisers, the protein content of pastures has been largely increased in some areas. It has been suggested that this may cause abnormal or incomplete synthesis of protein during the period of rapid pasture growth and that this in turn might cause the production of toxic pre-protein substances at the time of year (June) when grass disease is most prevalent. Systematic chemical investigations of the important nitrogenous constituents of pasture are being carried out. Many samples of soil from affected pastures have been examined as well as samples of grass but so far no correlation has been found between the type of soil or grass and the occurrence of the disease.

Animals may develop grass sickness after having been out at grass for only very short periods and in such cases the hypothetical toxic agent would have to be present in very high concentration. To meet this objection it was suggested that the toxic agent may persist in hay but against this view is the fact that the disease practically never occurs in horses in towns within grass sickness areas although they are fed hay from affected pastures. Pastures have been analysed for such special toxic substances as icterogenin, cyanide and oxalate. No substance resembling icterogenin was isolated and the cyanide content of affected pastures was far below the toxic level. Some pastures, especially those containing abundant sheep's sorrel, were rich in oxalate. Administration of cyanide and oxalate to horses failed, however, to produce symptoms resembling those of grass sickness and icterogenin was without effect. The hypothesis that the disease is caused by a toxic substance elaborated in the pastures thus finds no support.

6. *Living Infective Agents.*—(*a*) Invasive bacteria.—A diplostreptococcus isolated from an acute case of grass sickness by Gaiger was at one time suggested as being the causal agent but it was later established that it was without aetiological significance. Numerous attempts to cultivate bacteria from the blood of affected horses have yielded uniformly negative results and no organisms of significance have been isolated from the peritoneal cavity, liver or spleen. Tocher claimed to have isolated *Clostridium botulinum* from a case of grass sickness but the view that this organism is related to the disease has not been confirmed by subsequent workers.

Attempts to transmit the disease to healthy horses have always proved unsuccessful, even when transfusion of large quantities of blood from animals with acute grass sickness has been used. The results of all transmission experiments have been negative, no matter what the material or route of inoculation.

(*b*) Protozoan parasite.—No protozoa have as yet been demonstrated in the blood or tissues of affected animals. If a protozoan parasite were involved it would probably be transmitted by a living vector, the most likely being an insect. The only blood sucking insects known to be parasitic on horses in affected areas during the month of June are *Stomoxys calcitrans* and *Haematopota pluvialis*. These flies do not survive low temperatures, however, making it difficult to explain the occurrence of cases of grass sickness during winter months. It should also be pointed out that the symptoms do not resemble those of any known protozoan disease.

(*c*) Toxin producing bacteria.—No worker other than Tocher has isolated *Cl. botulinum* from the spleen of affected animals and available evidence is against the view of its significance. Administration of the toxin of this organism (Type B) to horses by stomach tube caused acute botulism but the symptoms were quite different from those of grass sickness.

In 1933 it was found that a small number of acute cases of grass sickness yielded the type D toxin of *Clostridium welchii* from the intestinal contents and similar results were obtained during each of the three succeeding years. All attempts to reproduce the disease, however, by administration of the toxin to horses were unsuccessful. In 1937 an extensive controlled experiment was undertaken in which approximately 1,000 horses were immunised against this toxin and a similar number of animals on the same farms were left as controls. A vaccine of high immunising properties was used and three doses were given at intervals of a fortnight. The results failed to show that vaccination conferred any protection against grass sickness although blood examination showed a good immunity response to the specific toxin. There is thus no evidence that a bacterial toxin is the cause of grass sickness.

(*d*) Filterable viruses.—The main objection to the view that a filterable virus is the causal agent would seem to be the epizoötiology of the disease. The characteristic symptoms of grass sickness seem to be due to irreparable nerve damage and the hypothetical virus would presumably be a neurotropic one. No lesions have been demonstrated in the central nervous system of affected horses but it may be that the virus is localised in its effects to the visceral nerves. There are various ways in which such a virus might be transmitted:—

1. By a living vector. The extensions of the disease up river valleys and from one farm to another on the coast suggest a living vector—mammal, bird or insect—and the conditions appeared to be satisfied by a small unwinged but motile insect, *Sminthurus viridis*, a member of the Order Collembola. This insect is especially numerous on pastures where grass sickness appears in epizoötic form and its numbers have increased considerably since the practice of sowing white clover, on which it lives, became common. This, as previously mentioned, was about the time (1910) when grass sickness was first recognised as being of importance. Administration by various routes of sweepings of affected pastures, containing large numbers of these

insects, as well as the use of extracts of the insects, failed to reproduce grass sickness.

In view of the occurrence of the disease in winter it seems unlikely that blood-sucking flies are concerned as vectors. It is possible that a wild mammal could act as a vector but up to now there is no evidence that this is so.

2. By ingestion. Ingestion of a hypothetical virus in the food and its entry by the pharyngeal mucosa is a possible method of infection.

3. Direct and droplet infection. The frequent occurrence of two or more cases on one farm at the same time suggests that direct contact or droplet infection might be the method of transmission, the virus gaining access through the pharyngeal mucosa or the olfactory nerve endings. On the other hand, cases occur sporadically on farms which are widely separated and with no evidence of direct or indirect connection.

4. Fomites. There is no evidence that any inert substance acts as a means of disseminating the infective agent.

Anterior poliomyelitis of man shows certain epidemiological features which are similar to those of grass sickness. For example, cases may occur in an epidemic area in a very erratic manner, individual cases developing at different places within the same affected area all at about the same time. The epidemic prevalence of the two diseases is extremely irregular and poliomyelitis, like grass sickness, occurs mainly in the summer and early autumn, although sporadic cases are met with during the winter months. Another virus disease with a closely limited seasonal incidence is Borna disease but in this case the blood is infective and infection can be transmitted by mosquitoes: in Borna disease, therefore, the seasonal incidence may be governed by climatic factors limiting the activities of the insect vectors.

The author concludes by expressing the view that "... there appears to be proper reason for excluding grass sickness from each of the disease groups, with the exception of that of virus disease, into which it might fall if only by a process of elimination of other possibles. There would appear to be, in fact, no grounds of objection to the assumption that its cause is a virus, except that its mode of transmission is very difficult to conceive. This same difficulty however obtains in the case of anterior poliomyelitis, which, although known to be caused by a filterable virus, is transmitted by means that are very imperfectly understood."

[The reader, like the abstractor, may be unwilling to accept this view of a virus as the most likely cause. Some of the discarded hypotheses have as much to recommend them and at least one of them, toxic substances developing in the pasture, appears to be still under investigation. The possibility that in grass sickness there occur abnormal chemical changes in the alimentary tract which may be associated with the clinical symptoms is an aspect which would seem to call for study by the biochemist and physiologist. It would seem advisable, therefore to leave open the question as to the nature of the causal agent of grass sickness and continue to investigate any and every possibility which appears feasible.—*Abstractor.*]

E. G. W.

ARTIFICIAL INSEMINATION CONTROL

Mr. Hudson has submitted to the House of Commons The Agriculture (Miscellaneous Provisions) Bill which, amongst other matters, seeks to control artificial insemination, a subject upon which the Minister some time ago promised legislation so that there should be uniformity of action on a matter of far-reaching importance.

Under clause 16, the Minister will be able to make regulations to control the practice of artificial insemination and to prohibit (subject to exemptions) the distribution and sale of semen of any animal except under licence. Such regulations may apply to cattle, sheep, goats, swine, horses, domestic fowls, turkeys, geese and ducks.

Licences will also be required under the regulations for the importation and exportation of semen.

Where a licence is held, premises may be entered by the Ministry officers and inspected, and tests may be carried out.

* * * * *

Weekly Wisdom

"*A good teacher must have, first, enthusiasm, that deep love of a subject, that desire to teach it and extend it without which all instruction becomes cold and lifeless; secondly,* a full personal knowledge of the branch taught; *not a second-hand information derived from books, but the living experience derived from the experimental and practical work in the best laboratories.*"—Professor Wood-Jones.

QUESTIONS IN PARLIAMENT

Marginal Land Cultivation: Hill Sheep Subsidy

Mr. Hughes asked the Minister of Agriculture whether assistance is to be given to hill farmers and other marginal producers in England and Wales, similar to that recently announced by the Secretary of State for Scotland, in respect of marginal production in Scotland?

Mr. T. Williams: Yes, Sir. Arrangements have now been made to afford to farmers in England and Wales assistance similar in character to that announced on November 17th for Scottish producers by my right hon. Friend the Secretary of State in reply to the hon. Member for Kinross and West Perth. (*Vide infra.*) I append a statement giving details of the measures proposed.

Following is the statement:

Consideration has been given to the difficulties confronting hill farmers in England and Wales and the Government has decided that further measures are necessary in order to enable hill lands to make a more effective contribution to food production and to preserve foundation stocks of cattle and sheep. Somewhat similar proposals for Scotland were announced by the Secretary of State for Scotland on November 17th. At this stage in the war it has become essential to look to the less favourably placed lands of the marginal type, which are common in hill districts, for part of the further expansion of output that is required of home agriculture.

Hill sheep farmers have already been given a subsidy for breeding ewes. As my right hon. Friend the Secretary of State for Scotland has just announced, this subsidy will be paid for a further year at the rate of 8s. per eligible ewe in the flock on December 4th, 1942. The conditions of eligibility will generally follow those in force during the past year. In special circumstances applications for payment on the number of ewes in the flock on December 4th, 1940, will be considered. Flocks producing cross-bred or half-bred lambs and maintained by purchase of ewes, shearlings or ewe lambs of mountain breeds, have in the past year generally failed to qualify for the subsidy. The lambs secure a higher price than the small lambs derived from pure Mountain breeds of sheep, but it is recognised that many of these producers are in need of assistance and it is proposed that in the coming year eligible applicants should receive a subsidy at half the standard rate.

In order to encourage the improvement of hill grazings in England and Wales and the provision of summer pasturage for young cattle from lowland dairy and other farms, a grant of £3 per head will be payable to the owner of the cattle in respect of all home-bred cattle kept on hill grazings for at least six months in the year. The cattle may be cows, heifers or steers, but must be of a hardy type. Bulls and calves will not be eligible. The farm must not be less than 50 acres in extent and at least 50 per cent. of the area must consist of rough hill pastures, taking into account grazing rights. Agisted cattle will be eligible, in the expectation that lowland farmers will thereby be encouraged to place on the hills replacement stock, including in-calf heifers. Applicants will have to satisfy their County War Agricultural Executive Committee that the hill grazings are likely to be improved and they must be prepared to undertake any necessary measures of improvement, such as surface draining, bracken cutting, or re-seeding. It is considered that this grant will enable the hill farmer to increase materially the productive capacity of hill land and at the same time will secure an expansion of home breeding of cattle.

These grants for hill sheep and upland cattle should enable most of the marginal farmers in the upland and hill districts to make their contribution to increased home food production. For those marginal farmers in other districts, who produce arable crops, the acreage payments for wheat rye and potatoes will provide some degree of security against the danger of low yields due to bad weather or other causes. In the main, therefore, those various payments will meet the difficulties of marginal farmers at the present time. It is recognised that there may be exceptional cases where the County War Agricultural Executive Committee will desire to direct an occupier to carry out some agricultural operation that is dictated by the requirements of the food production campaign, but which the occupier could not carry out from his own unaided resources without making his farming enterprise as a whole on the farm in question uneconomic. If a case for assistance is established it will be given in the form of a remission of part of the cost of such goods or services as the Committee may consider it necessary to supply to the farmer to assist him to perform the operation in question.

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Hill-Sheep Subsidy: Scotland

Mr. Snadden asked the Secretary of State for Scotland the scale of assistance to be granted to breeders of hill-sheep in respect of the year 1942?

Mr. Johnstone: The Government have carefully considered the question of assistance to hill-sheep farmers in the United Kingdom for the present year. Taking all the circumstances into account, they have decided to make a payment of 8s. per breeding ewe. The conditions of payment to Scottish farmers will be broadly the same as those operating last year. Payment will be based on the number of breeding ewes in the flock at December 4th, 1942, but a farmer may appeal in special circumstances for payment to be made on the number of such ewes as at December 4th, 1940.

Mr. Snadden: Can the right hon. Gentleman say whether there will be a ceiling?

Mr. Johnstone: Yes, Sir. The fixed price is 8s. per breeding ewe.

Sir Waldron Smithers: In view of the fact that the right hon. Gentleman has answered on behalf of the Government, can he say whether this will apply to export sheep as well?

Mr. Johnston: Yes, Sir. I have answered on behalf of the Government. It will apply to all British hill-sheep.

. . . . .

Swill (Sterilisation)

Mr. Higgs asked the Minister of Agriculture what steps he has taken to ensure that swill is sterilised before distribution from camps and other points of Government concentration where large quantities are always available?

The Minister of Agriculture (Mr. R. S. Hudson): The Departments concerned have agreed that swill from Service establishments should wherever practicable be sterilised by concentration or boiling before disposal to stock keepers, and appropriate arrangements are being made as quickly as practicable.

. . . . .

Dogs (Quarantine)

Sir R. Gower asked the Minister of Agriculture whether, in view of the importance of the regulations relating to the quarantine of dogs coming from abroad, in preventing the reintroduction of rabies into this country, he is satisfied that the machinery for enforcing them is working satisfactorily?

Mr. Hudson: I am satisfied that at present the regulations which require dogs brought from abroad to be detained in quarantine are being properly enforced. I realise, however, that when the time arrives for troops and other personnel to return to this country in large numbers, the problem may become more complex and I am therefore keeping the matter in mind.

. . . . .

Horses (Ill-Treatment)

Colonel Carver asked the Minister of Agriculture whether, in view of the growing number of cases of ill-treatment of horses, due largely to ignorance, he will cause the war agricultural executive committees to warn horse owners and users generally against such action?

Mr. Hudson: I am not aware of such cases. The second part of the Question does not, therefore, arise.

. . . . .

Milk Yields

Sir A. Baillie asked the Minister of Agriculture whether he is aware that indifferent winter milk yields are mainly due to insufficient feeding of cows and heifers in the six weeks before calving; and whether this will be remedied by increased rationed food?

Mr. Hudson: I am well aware of the need for adequate feeding of cows and heifers before calving, but I cannot altogether accept that the position is as stated by my hon. and gallant Friend. Dairy herds receive priority in rations and special provision is made for in-calf animals.

Mr. Loftus: Is my right hon. Friend aware that dried grass is the finest possible food for cattle and that a great deal of it is available, but is not being used, in the aerodromes of the country?

. . . . .

Milk (Pasteurisation)

Sir R. Gower asked the Minister of Health whether he has considered the letter sent to him by the hon. Member for Gillingham with regard to a product which can be mixed with milk to make it self-sterilising; and whether he will investigate this question before proceeding any further with the schemes for compulsory pasteurisation?

Mr. E. Brown: Yes, Sir. The letter suggests that all milk should be bottled on the farm and states that researches are being made with a view to obtaining a product from seaweed to be mixed with milk. Apart from any other considerations which may arise, it is, in my view, most undesirable that preservative substances should be added to food if they can be avoided, and in view of the established merits of pasteurisation, I should not be prepared to delay any measures which may otherwise be found desirable, on account of the investigations referred to.

Agriculture: Long-term Policy

Mr. De la Bere asked the Minister of Agriculture whether he will now reconsider his decision in connection with making a pronouncement on Government long-term policy for agriculture, and give an assurance that he will do this early in 1943?

Mr. Hudson: No, Sir.

Mr. De la Bere: Is the right hon. Gentleman aware that verbal promises were given to the farmers, and is he aware of the tremendous efforts they have made in the national interest? Would it not be in the national interest that some definite scheme should be announced?

Mr. Hudson: The answer to the first two parts of the Question is in the affirmative and to the last part in the negative.

. . . . .

On Thursday of last week the House adjourned for the Christmas Recess.

ROYAL COLLEGE OF VETERINARY SURGEONS

Membership Examinations (December, 1942)

LIST OF SUCCESSFUL CANDIDATES

(*Continued from page* 535)

Glasgow (continued)

Third Year:

Bannatyne, C. C.	Johari, M. D. (A)
Brownlie, J. F.	Mitchell, David
Campbell, D. T. J.	Moodie, Miss M. P.
Doran, G. F. P.	Muir, T. H.
Forsyth, Harry	Porter, E. V. H.
Foster, A. H.	*Roberts, R. M.
Gregg, J. R.	Sillars, David
Howie, T. W. T.	Sumner, K. C.
Hukku, R. N.	Weissberg, E.
Jarvis, Thos.	Williamson, J. B.

* denotes 2nd class honours.
(A) denotes credit in Anatomy.

Fourth Year:

Bell, A. K.	Hall, David
Buchanan, W. G.	Hughes, H.
Buntain, David	Johnston, W. G.
Campbell, Miss D. G.	McCallum, F. J.
Clow, D. G.	Mackenzie, G. J.
Dewar, H. D.	Noble, W. N.
Fraser, J. R.	Rankin, W. L.
Gaston, Miss D. A.	Thomas, E. V.

Edinburgh

First Year:

Currie, R. K.	Scott, A. M.
Noble, Claude	Simms, I. H.
Philip, H. M.	Wharton, M. H. (B)
Price, E. L.	

(B) denotes credit in Biology.

Second Year:

Allan, Duncan	Low, R. J.
Brown, D. A.	Mackenzie, F.
Dudgeon, Alex.	Rimmer, S. M.
Handy, D. E.	Shearer, G. C.

Third Year:

Boyle, J. G. S.	Oxley, Harry
Harkness, B. R.	Richter, W. A. G.
Macdonald, Angus	Wood, James

Fourth Year:

Cox, R. L.	Pearson, R. G.
Dougill, G. P.	Sutherland, D. J. B.
Dougill, John	Thomson, W. W.
Dymock, W. H.	Walker, I. A.
Macnaughton, R. R.	Walker, K. A.
Mackinnon, M. M.	Wishart, Graham
Naismith, R. S.	

Final Year:

Allen, T. H.	Ironside, C. J. T.
Chisholm, L. P. S.	Lowes, Emerson
Daniell, G. H.	Mackay, Robt.
Ellse, J. B.	Mackintosh, A. S.
Evans, R. P.	McTaggart, H. S.
Gracey, J. F.	Mason, George
Greenwell, G. E.	Parker, W. H.
Guilbride, P. D. L.	Pearson, J. K. L.
Hughes, E. E.	Rogerson, Thomas
Hunniford, J. N.	Shaw, W. B.
Hutchinson, R. A.	Smith, D. C.
Inglis, J. W. C.	Tallantire, I. W.

(*To be concluded*)

NOTES AND NEWS

The Editor will be glad to receive items of professional interest for inclusion in these columns.

Diary of Events

Dec. 28th, 1942.—Changes of Address for 1943 Register to be reported to Registrar, R.C.V.S., 18, Victoria Avenue, Harrogate.

Jan. 1st, 1943.—Meeting of the Joint Veterinary Officers and Public Health and Parliamentary Committee, N.V.M.A., 11.15 a.m.; Finance and General Purposes Committee, 2.45 p.m.

Jan. 5th and 6th, 1943.—First Annual Conference of the Veterinary Students' Association of Great Britain and Eire, at the Royal Veterinary College, Streatley, nr. Reading.

Jan. 6th, 1943.—Meeting of the Editorial Committee, N.V.M.A., 2.30 p.m.

Jan. 12th, 1943.—R.C.V.S. Committee Meetings, Royal Station Hotel, York.

Jan. 13th, 1943.—R.C.V.S. Committee and Council Meetings, York.

Jan. 16th, 1943.—Meeting of the Society of Women Veterinary Surgeons at Birmingham.

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R.C.V.S. COUNCIL ELECTION

The Council having been empowered, by the Privy Council, to fill the casual vacancies caused by the deaths of Col. G. K. Walker and Major G. W. Dunkin, and the resignation of Mr. A. Mackenzie, a vote has been taken and the following members have been declared duly elected:—

For the period ending June, 1944:—
Mr. S. J. Motton,
Mr. W. R. McKinna;
For the period ending June, 1943:—
Brigadier C. A. Murray.

* * * * *

PERSONAL

Appointments.—The following first appointments in the Colonial Veterinary Service are announced: Mr. J. F. A. Sprent, B.Sc., M.R.C.V.S. as Veterinary Research Officer, Nigeria; Mr. I. H. Pattison, B.Sc., M.R.C.V.S., as Veterinary Officer, Palestine.

* * * * *

Births.—Bell.—On October 13th, at Kampala, Uganda, to Margaret (*née* Winter), wife of F. R. Bell, B.Sc., M.R.C.V.S., a daughter.

Randle.—On December 8th, 1942, at Newport, Isle of Wight, to Dorcas, wife of C. S. Randle, M.R.C.V.S., a son—Alan John.

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SOCIETY OF WOMEN VETERINARY SURGEONS

As Miss Bentley—so we learn with regret—has had a recurrence of her recent illness and is unlikely to be fit for some weeks ahead, we are asked to announce that Mrs. E. J. Thomson has very kindly consented to become Acting Secretary *pro tem.* of the above Society.

Will members please note and until further notice address all correspondence to Mrs. E. J. Thomson, 29, Celtic Avenue, Shortlands, Kent.

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ROYAL ARMY VETERINARY CORPS

Mention in Despatches

Announcement is made in the issue of *The London Gazette* dated December 11th, 1942, that the King has been graciously pleased to approve that Major A. V. Franklin be Mentioned in recognition of gallant and distinguished services in the Middle East during the period November, 1941, to April, 1942.

* * * * *

FOOT-AND-MOUTH DISEASE IN SCOTLAND

Scotland, after receiving an "all clear" signal from foot-and-mouth disease infection only as from the morning of December 10th (when the Lanarkshire restrictions were removed) was once more involved on December 12th, owing to an outbreak which was confirmed at Forres, the first time Morayshire has had such a visitation for about 70 years. Aberdeenshire, it will be recalled, had an outbreak early this year. The fact that Morayshire, so far removed from the Forth area and from Hamilton, the seats of the recent outbreaks, should be involved, emphasises the need for the strictest care in the handling of swill that is being fed to stock. Not only should swill be boiled effectively before being fed, but there is need for every care that no stock is allowed near to swill-containers arriving at farms. Centralised boiling of swill is the safest method, but this may not be possible in all parts of Scotland, though that course is being pressed by both stockowners and central authorities.

As we have reason to suppose that certain of the mail destined to reach us on Saturday, December 19th, failed to do so, we should be grateful if veterinary surgeons who wrote to us on December 17th or 18th would kindly repeat their order and enquiries.—Bayer Products, Ltd., Africa House, Kingsway, London, W.C.2.

CORRESPONDENCE

Letters to the Editor should reach the Office not later than by the first post on Monday morning for insertion in following Saturday's issue.

The views expressed in letters addressed to the Editor represent the personal view of the writer only and must not be taken as expressing the opinion or having received the approval of the N.V.M.A.

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GRASS DISEASE IN HORSES

Sir,—In *The Veterinary Record*, Volume 54, 1942, page 31 I read an article on "Suspected grass disease in Northamp shire" by W. A. Dickinson. I have been following the liter on grass disease and frequently wondered whether there is a possibility that some of the cases described as grass disease ma be cases of Senecio or Trifolium poisoning. The cases describ by Dickinson, in some aspects at least, closely resemble Sen disease in horses as we know it in South Africa. The difference is that Dickinson apparently saw no pathological chan in the liver, but I am wondering whether he paid particular atten tion to this organ.

Yours faithfully,
D. G. Steyn.

Section of Pharmacology and Toxicology,
Division of Veterinary Services,
Onderstepoort.
October 7th, 1942.

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TUBERCULOSIS IMMUNISATION IN ANIMALS

Sir,—On page 401 in the issue of *The Veterinary Record* of October 3rd, under the heading of "Bovine Tuberculosis in Germany," there appears the following under paragraph 5, "Immunisation":—

"It appears to be the current German opinion that there is no hope of immunising animals against tuberculosis. Dr. Bruno Lang, an authority on human tuberculosis, recently declared himself in that sense. B C G appears to be discredited in Germany, and is rarely mentioned now in veterinary papers."

The above statement seems to bear out exactly the conclusion that I came to after trying the vaccine for 14 years in my own herd. Dr. Watson, of Ottawa, also came to the same conclusion.

Yours faithfully,
Graham Rees-Mogg.

Clifford Manor,
Stratford-upon-Avon.
December 12th, 1942.

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ANTIRACHITIC ADDITIONS TO POULTRY MASH

Sir,—In looking through *The Veterinary Record* dated October 24th, I came across the letter written under the above title. In view of the importance of the issue raised and of the effect the letter referred to will have on practising veterinarians with regard to the use of cod-liver oil, I should like to bring a few facts bearing on the issue in question before your readers.

Firstly, cod-liver oil supplies are short, and in the national interest every care should be taken to avoid squandering such supplies as are available.

Secondly, if a chick diet contains less than 0·7 per cent. calcium and 0·4 to 0·5 per cent. phosphorus rachitic symptoms are bound to arise, and under such circumstances the provision of extra cod-liver oil will not affect a cure.

Thirdly, the form of vitamin D present in cod-liver oil is fully effective both for the rat and the chick.

Fourthly, I have analysed several chick mashes in recent months and have found the calcium content to be below the minimum indicated above, and have also personally investigated two cases of rickets in which the trouble was found to be due to a shortage of calcium and not to lack of vitamin D.

In view of these facts, I consider that the advice given in the Ministry of Agriculture's News Service and quoted in the *Record* dated October 10th, 1942, fully justified, and I hope that veterinary practitioners called in to cases in which 1 per cent. of cod-liver oil or controlled cod-liver oil mixture is included in the diet will pay due attention to the possibility of a shortage of calcium being the cause before prescribing lavish doses of cod-liver oil as a possible remedy.

Yours faithfully,
E. T. Halnan.

Poultry Nutrition Section,
Animal Nutrition Institute,
Cambridge.
December 19th, 1942.